

REMARKS

I. Status of the Claims

Upon entry of this Amendment, claims 1, 3-47, 53 and 54 are pending. Claims 2, 48 and 52 have been cancelled without prejudice or disclaimer.

Claim 1 has been amended to add a period at the end of the claim. Claims 3-19 have been amended to depend from claim 1, subsequent to cancellation of claim 2. Claim 53 has been amended to depend from claim 1, subsequent to cancellation of claim 52. The scope of claim 53 is believed to be unchanged.

By this Amendment, no new matter has been added to the application.

II. Response to Rejections

The rejections set out in the Office Action are summarized and addressed as follows.

(i) Rejection Under 35 U.S.C. §112, first paragraph (enablement)

Claims 48 and 52 were rejected for alleged lack of enablement. In response, without conceding the validity of the rejections, claims 48 and 52 have been cancelled, without prejudice or disclaimer. The rejection of claims 48 and 52 is thus moot.

(ii) Rejections Under 35 U.S.C. §112, second paragraph

The Examiner has rejected claims 1, 2, 22, 25, 28, 31 and 34 for alleged indefiniteness. In response, claim 1 has been amended to add a period and claim 2 has been cancelled. The rejection of claim 1 has thus been addressed and the rejection of claim 2 is moot.

The rejection of claims 22, 25, 28, 31 and 34 for indefiniteness as being respective duplicates of claims 3, 7, 10, 14 and 17 is traversed because the respective pairs of claims differ in scope. Claims 3, 7, 10, 14 and 17 are thus directed generally to a crystalline form of compound 1 whereas claims 22, 25, 28, 31 and 34 are directed to “[s]olid compound I

containing a crystalline Compound I" form. *See* respective base claims 20, 23, 26, 29 and 32. Claims 3, 7, 10, 14 and 17 are thus not respective duplicates of claims 22, 25, 28, 31 and 34.

Reconsideration of the claims and withdrawal of all rejections under 35 U.S.C. §112, second paragraph is requested.

(iii) Rejection Under 35 U.S.C. 102(b)

Claims 1-48 and 52-54 have been rejected as being allegedly anticipated by Kaneko et al., *J. Med. Chem.*, 1997, 40:1863-1869 ("Kaneko"). The Examiner's position is that Kaneko discloses the claimed Compound I (Kaneko's Compound (8)), and that although Kaneko is silent as to whether or not Compound (8) is a crystalline form, the Examiner nonetheless assumes this to be the case. The Examiner thus asserts that Kaneko anticipates each of claims 1-48 and 52-54. The Examiner's analysis of Kaneko is flawed, however, in that the Examiner has no basis for asserting that Kaneko's Compound (8) is present in crystalline form. The rejection is thus traversed on the grounds that Kaneko fails to disclose crystalline Compound I, as called for in the claims.

It is noted at the outset that the Examiner has made apparently inconsistent statements and arguments concerning the physical state of Kaneko's Compound (8) vis a vis the pending claims. On page 5 of the Office Action, the Examiner thus states that, "The reference shows the compound, but is silent on the particular **crystalline** form" and "In this case, the 'unknown property' is the particular **crystalline** form." (emphasis in original) These statements suggest the Examiner construes the claims to be directed to crystalline forms of Compound I and Kaneko to be silent as whether Compound (8) is crystalline, but that the property of being crystalline is inherent to Compound (8).

In an apparent reversal of the interpretation set out above, however, on page 6 of the Office Action, after stating the missing element in the prior art is crystalline Compound I, the Examiner states, "Again, the 'CHARACTERISTIC' which the prior art is silent on is the amorphous form." On page 8 of the Office Action, the Examiner further states, "Overcoming the rejection is very straightforward. One simply replicates the prior art procedure. If the amorphous form does not appear at all in the product, or if on repetition it sometimes does not appear in the

product, then the rejection is overcome." These statements would be applicable if the claims were directed to the amorphous form of Compound I.

The Examiner has thus made apparently inconsistent statements that are applicable to the mutually exclusive possibilities that the claims are directed to crystalline forms of Compound I and the amorphous form of Compound I. The claims are in fact directed to crystalline Compound I. Applicant thus responds to the instant rejection based on the Examiner's assertion that the characteristic of being crystalline is inherent to Kaneko's Compound (8). The rejection should be withdrawn because there is no basis for asserting the characteristic of being crystalline is inherent to Kaneko's Compound (8).

The Examiner thus has no basis for asserting Kaneko discloses Compound I in crystalline form, particularly the alpha, beta, gamma, delta and epsilon forms of Compound I that are disclosed in the specification and claimed. As set forth in the specification, these respective crystalline forms of Compound I are obtained through a series of deliberate crystallization steps, with variations in crystallization conditions leading to the different crystalline isoforms. Kaneko's Compound (8), in contrast, was purified from crude product by column chromatography, without any crystallization step. See Kaneko at page 1867, section entitled "General Procedure for Formation of (Alkoxymethyl)- and [(alkylthio)methyl]-K252a Derivatives" (setting forth a procedure for formation of Compound (13) and stating "Compounds 6-12 are prepared by the general procedure described for 13."

A comparison of the melting points of Compound (8) versus the melting points of alpha, beta, gamma, delta and epsilon further demonstrates that Compound (8) does not include any of these crystalline forms. Compound (8) thus has a melting point of 163-165°C (Kaneko at page 1867) which is very different from the melting points for each of alpha (182.4, 188.9 or 183.7°C, depending on method of preparation), beta (211.7), gamma (218.0 or 214.2), delta (212.1 or 221.6) or epsilon (181.8).

In short, the present application discloses that obtaining particular crystalline isoforms of Compound I is highly dependent upon crystallization conditions, whereas Kaneko fails to even attempt to crystallize Compound (8) and, moreover, Kaneko's Compound (8) has a

melting point that is very different from the melting points of the claimed crystalline forms of Compound I. There is thus no basis for the Examiner to assert that Kaneko's Compound (8) includes any crystalline form of Compound I and, particularly, no basis for the Examiner to assert that Kaneko's Compound (8) includes any amount of the alpha, beta, gamma, delta or epsilon crystalline forms of Compound I. For at least this reason, the rejection of the subsisting claims as anticipated by Kaneko should be withdrawn.

Furthermore, in view of the arguments set out above, there is no basis for the Examiner to require that the Applicants show that the claimed crystalline Compound I is different from Kaneko's Compound (8). As set forth above, the claimed compounds are obtained under particular crystallization conditions whereas Kaneko purifies Compound (8) by column chromatograph and without a crystallization step. Compound (8) is thus not "produced by identical or substantially identical processes" (*see* Office Action at page 8) as the claimed crystalline compounds. There is thus no basis for asserting the prior art discloses the claimed compounds and in the absence of such a basis the Examiner has no grounds for requiring the Applicants to perform tests to show the claimed compounds differ from the prior art.

For at least the reasons set out above, the rejection of subsisting claims 1, 3-47, 53 and 54 as being anticipated by Kaneko should be withdrawn.

With further respect to claims 35-37 and 42, these claims are directed to a method of preparing crystalline Compound I from methanol. Kaneko fails to disclose the claimed method. For this reason additionally, Kaneko fails to anticipate claims 35-37 and 42.

With further respect to claims 53 and 54, these claims are directed to methods of treating the conditions of Parkinson's disease, Alzheimer's disease, Huntington's disease, peripheral neuropathy or AIDS dementia. Kaneko fails to disclose treatment of any of these conditions. For this reason additionally, Kaneko fails to anticipate claims 53 and 54.

For all of the reasons set out above, the subsisting claims are not anticipated by Kaneko. Reconsideration of the claims and withdrawal of all rejections under 35 U.S.C. 102(b) is requested.

Applicant : Ole Nielsen et al.
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Page : 16 of 16

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III. Conclusion

This application is believed to be in condition for allowance, which is earnestly solicited.

Respectfully submitted,

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